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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

NOTIFICATION DATE	DELIVERY MODE
05/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/726,198	JOHN ET AL.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/12/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-50* is/are rejected.

7)☒ Claim(s) *49 and 50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/12/2009 has been entered. Claims 1-37 have been cancelled and new claims 38-50 have been added and are under consideration.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 38-44, 48 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Seetharaman et al. (Journal of Biological Chemistry, 1998 273: 13047-13052), as evidenced by SCORE search results 20070105_174341_us-10-726-198-1.50 aligns.rup and LEG3_HUMAN alignment) essentially for the reasons set forth in section 17- pages 19-20 of the Office Action of March 8, 2007.

Examiner argued that:

It is noted that the recitation of the uses of the composition in claims 3, 4, and 7 are merely suggestive of intended uses and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which is N-terminally truncated galectin-3 which has a sequence according to SEQ ID NO: 1 and analogues thereof.

It is noted that the specification teaches in the brief description of Figure 2 that N-terminally truncated galectin-3 is galectin-3C (see p. 14, lines 10-14).

Seetharaman et al. (J. Biol. Chem. 1998 273:13047-13052) teach galectin-3C which consists of residues 107-250 of human galectin-3 (see p. 13047, right col., *Protein Purification and Crystallization*). One of skill in the art would immediately envision putting galectin-3C in a pharmaceutically acceptable carrier like phosphate buffered saline for the storage and use of the protein.

Applicants argue that note that new claims 38-50 overcome rejections based on Seetharaman. Seetharaman fails to recite wherein truncated galectin-3 is Leu-7 to Ile-143 of SEQ ID NO: 1, as recited in new independent claim 38.

Applicants' arguments have been considered, but have not been found persuasive as the new claims are not limited to a truncated galectin-3 protein consisting of residues 7-143 of SEQ ID NO: 1, but encompass proteins comprising these sequences of SEQ ID NO: 1, which the protein galectin-3C protein of Seetharaman et al does. Additionally, it is noted that formulating the composition is merely suggestive of intended use and is not given weight for purposes of comparing the claims with the prior art. Furthermore, a conserved amino acid substitution of Val-95 of SEQ ID NO: 1 would encompass the valine itself. Furthermore, one of skill in the art would immediately envision putting one or more additional agents in the composition such as a preservative or stabilizer.

It is noted that the product of the prior art comprises the same product as claimed in the instant invention, a protein comprising the truncated galectin-3 which begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1, thus the claimed product is anticipated

because the product will inherently be effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the galectin–3C is effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

3. Claims 38-44, 48 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Gitt et al. (J. Biol. Chem. 1995, 270:5032-5038) essentially for the reasons set forth in section 8, pages 12-14 of the Office Action of December 12, 2008.

Examiner argued:

It is noted that, given their broadest reasonable interpretation the claims are drawn to proteins that comprise the recited N-terminal truncations with varying identity to the sequence of SEQ ID NO: 1 claimed.

It is noted that the recitation of the uses of the composition in claim 7 is merely suggestive of intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which are the proteins comprising the claimed N-terminally truncated galectin-3.

Gitt et al. teach rat galectin-5, which has a conservative substitution of isoleucine for valine at position 95 of SEQ ID NO: 1, see Fig. 3 and Appendix 1. Gitt et al. teach also teach rat galectin-3 which is a protein that comprises the claimed galectin-3 trucations of claims 1, 3, 4, 7, 27-34 and 37, see Fig. 3 and Appendix 1. One of skill in the art would immediately envision

putting galectin-5 in a pharmaceutically acceptable carrier like phosphate buffered saline for the storage and use of the protein.

Although the reference does not specifically state that galectin-5 is effective to reduce tumor size or metastasis in breast cancer, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicants argue that Gitt fails to teach "A composition consisting of N- terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1...", elements of new independent claim 38. Moreover, Gitt fails to teach compositions of truncated forms of SEQ ID NO: 1, for example, removing the amino terminal amino acids of SEQ ID NO: 1 as in independent claim 38. Applicants argue that the third full paragraph of column 2 page 5037 of Gitt where Gitt recites "Of the other galectins that have been sequences, galectin-5 most closely resembles galectin-4 (Fig. 3)...This is especially true in the protein region defined by the exon that contains the majority of the conserved residues.., and that is known to interact directly with the carbohydrate ligand...In this region, galectin-5 and the second domain of galectin-4 have 54% amino acid identity. In contrast, comparable domains of galectin-1, -2, and -3 show 31, 37, and 48 % identities, respectively..." As demonstrated in Fig. 3 of Gitt, galectin-5 is not galectin-3, much less a truncated form of galectin-3.

Applicants' arguments have been considered, but have not been found persuasive as the new claims are not limited to a truncated galectin-3 protein consisting of residues 7-143 of SEQ ID NO: 1, but the claims encompasses a protein comprising a protein starting with Leu-7 and

extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143. Thus, the protein taught by Gitt is encompassed by the claimed protein. Additionally, one of skill in the art would immediately envision putting one or more additional agents in the composition such as a preservative or stabilizer.

It is noted that the product of the prior art comprises the same product as claimed in the instant invention, a protein comprising the truncated galectin-3 which begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1, thus the claimed product is anticipated because the product will inherently be effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the galectin–5 is effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

4. Claims 38-45 and 48-50 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No, 6,967,021 (Panjawani et al. April 27, 2001) essentially for the reasons set forth in section 9, pages 14-15 of the Office Action of December 12, 2008.

Examiner argued:

It is noted that the recitation of the uses of the composition in claim 7 is merely suggestive of intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which are the proteins comprising the claimed N-terminally truncated galectin-3.

It is noted that, given their broadest reasonable interpretation the claims are drawn to proteins that comprise the recited N-terminal truncations with varying identity to the sequence of SEQ ID NO: 1 claimed.

US Patent No, 6,967,021 teaches SEQ ID NO: 3, which has a conservative substitution of isoleucine for valine at position 95 of SEQ ID NO: 1 and comprises a galectin-3 truncation from proline 6 to serine-134, see Appendix 2. US Patent No, 6,967,021 also teaches galectin-3/SEQ ID NO: 1 which comprises the truncation mutants of the invention, see appendix 1. US Patent No, 6,967,021 contemplates pharmaceutical compositions with pharmaceutically acceptable carriers including polyethylene glycol, see abstract, col. 4-lines 3-30, and col. 14 lines 5-20 and 44-50. It is noted that the PEG derivative of galectin-3 in claim 25 is not limited to the PEG being attached to the galectin-3.

Although the reference does not specifically state that SEQ ID NO: 1 or 3 is effective to reduce tumor size or metastasis in breast cancer, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicants argue that on page 14, the Action asserts that "Claims 1-4, 7, 25 and 27-34 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,967,021 (Panjawani et al. April 27, 2001, [hereinafter "Panjawani"])...given their broadest reasonable interpretation the claims are drawn to proteins that comprise the recited N-terminal truncations with varying identity to the sequence of SEQ ID NO: 1 claimed... [Panjawani]...teaches SEQ ID NO:3, which has a conservative substitution of isoleucine for valine at position 95...and comprises a galectin-3 truncation from proline 6 to serine 134..." Applicants argue that claims 1-4, 7, 25 and 27-34 and 37 have been canceled.

Applicants argue that at Panjawani fails to disclose, "A composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu- 7 of S EQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: l," elements of new independent claim 38. The Applicants argue that that new claim 38 overcomes rejections based on Panjawani. Therefore, the Applicants request removal of the 35 U.S.C. § 102(b) rejection based on Panjawani. Additionally, claims 39-50 have all the elements of independent claim 38 plus additional elements, therefore rejection of claims 39-50 based on Panjawani are improper.

Applicants' arguments have been considered, but have not been found persuasive as the new claims are not limited to a truncated galectin-3 protein consisting of residues 7-143 of SEQ ID NO: 1, but the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143. Thus, the protein taught by Panjawani et al. is encompassed by the claimed protein. Additionally, Panjawani et al. teach adding anti-inflammatory agents to the pharmaceutical compositions of the invention, see paragraph bridging cols. 3 and 4. Additionally, in the absence of a limiting definition of derivatized with one or more PEG molecules, the PEG compositions of Panjawani et al. are encompassed by the claims.

Additionally it is noted that the product of the prior art comprises the same product as claimed in the instant invention, a protein comprising the truncated galectin-3 which begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1, thus the claimed product is anticipated because the product will inherently be effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically

state that the SEQ ID NO: 1 or 3 are effective to reduce tumor size, metastasis, induce death in cancer cells, inhibit inflammation, and inhibit symptoms of rheumatoid arthritis, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No, 6,967,021 (Panjawani et al. April 27, 2001) in view of Veronese (Biomaterials, March

2001, 22:405-17) essentially for the reasons set forth in section 10, pages 15 and 16 of the Office Action of December 12, 2008.

Examiner Argued:

US Patent No, 6,967,021 teaches as set forth above, but does not teach attaching PEG molecules to Cys-66 on SEQ ID NO: 1. US Patent No, 6,967,021 additionally teaches using galectin-3/SEQ ID NO: 1 for the treatment of epithelial wounds, see Abstract and claims.

Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, see p. 405-right col. Veronese teaches that PEG conjugation of a protein can maintain its biological functions while inhibiting antibodies, antigen processing cells, and proteolytic enzyme activities toward the protein, see p. 406-left col. Veronese teaches PEGylation of proteins using rare thiols like cysteine, see p. 410 and figure 9.

It would have been *prime facie* obvious for one of skill in the art to conjugate galectin-3/SEQ ID NO: 1 taught by US Patent No, 6,967,021 with PEG because Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, thus one of skill in the art would have been motivated to attach PEG as describe by Veronese to enhance the therapeutic potential of galectin-3/SEQ ID NO: 1 taught by US Patent No, 6,967,02 in the treatment epithelial wounds. One would have been motivated to attach the PEG molecules a Cys-66 as this is the only cysteine in galectin-3, truncated or full length.

Applicants argue that these 35 U.S.C. § 103(a) rejections are based on Panjawani in combination with Veronese. Therefore, once the impropriety of using Panjawani in the rejections is established, all rejections based on Panjawani in combination with other references must fall. Applicants argue that a prima facie case of obviousness requires: 1) some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or combine the teachings; 2) a reasonable expectation of success; 3) the prior art reference or references must teach or suggest all the claim limitations. As discussed above, Panjawani does not provide or suggest elements disclosed in new independent claim 38, notably "the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO:1" This deficiency is not made up for in Veronese. Therefore, rejection under 35 U.S.C. § 103(a) based on Panjawani in view of Veronese is improper.

Applicants' arguments have been considered, but have not been found persuasive because persuasive as the new claims are not limited to a truncated galectin-3 protein consisting of residues 7-143 of SEQ ID NO: 1, but the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143. Thus, the protein taught by Panjawani et al. is encompassed by the claimed protein.

New Grounds of Rejection

Drawings

6. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Fig. 4C. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 38-50 are rejected under 35 USC 112, first paragraph because the specification, while being enabling for a composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 **consists of SEQ ID NO: 1** and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to **reduce breast tumor size or reduce breast tumor metastasis**, *does not* reasonably provide enablement for a composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO:I and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to **reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered

in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to a composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO:I and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis. The broadest reasonable interpretation of the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143 that will be effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis.

The specification teaches that N-terminally truncated galectin-3/SEQ ID NO: 1 injected intramuscularly, twice daily reduced tumor volume and weight and tumor metastasis in mice injected subcutaneously with MDA-MB-435 human breast cancer cells that express galectin-3 (see Example 1, p. 48-56, and Figs. 6-9).

Additionally, the specification postulates that evidence suggests that in rheumatoid arthritis and juvenile idiopathic arthritis defective apoptosis of mononuclear phagocytic cells and activation of synovial fibroblasts is related to increased expression of galectin-3. The

specification hypothesizes that a potential therapeutic agent for arthritis could be based on the inhibition of galectin-3. The specification hypothesizes that soluble recombinant N-terminally truncated galectin-3 competes with endogenous galectin-3 for carbohydrate binding sites in the extracellular matrix and cell-cell adhesions important in cellular invasion process and activation of immune cells through cross-linking carbohydrate expressing receptors on cell surfaces by multimerization mediated by the N-terminal domain. The specification hypothesizes that in arthritis N-terminally truncated galectin-3 is expected to be therapeutic by reducing the threshold for induction of apoptosis in some cells of the immune system that express and absorb galectin-3 from the extracellular milieu, and to reduce the activation of other cells such as neutrophils and synovial fibroblasts (see p. 75, lines 12-25).

Additionally, the specification teaches that organ biodistribution analyses showed that N-terminally truncated galectin-3 localized to the liver, kidney, and spleen but not to the heart or lungs (see p. 54, lines 13-16, and Figure 5).

The teachings of the specification cannot be extrapolated to the scope of the claims because no nexus has been established between the claimed composition and treating rheumatoid arthritis, juvenile idiopathic arthritis, atherosclerotic cardiovascular disease and cancers, other than breast cancer, and 1) the claims encompass unknown and undefined variants and fragments of the N-terminally truncated galectin-3/SEQ ID NO: 1 and the unpredictability of predicting function from structure in protein biochemistry is well known in the art 2) the process of drug discovery is unpredictable and 3) cancers are heterogeneous in nature and 4) and the efficient targeting of diseased cells with the N-terminally truncated galectin-3C for treatment is unpredictable.

1) In particular, as drawn to predicting structure from function from structure in protein, Bowie et al (Science, 1990, 257:1306-1310, previously cited) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col. 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col. 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J. of Cell Bio. 111:2129-2138, 1990, previously cited) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252, previously cited) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Given the lack of teaching of amino acid residues critical to the

function of the claimed N-terminally truncated galectin-3, in view of the unlimited and undefined alteration in N-terminally truncated galectin-3 encompassed by the claims, the function of the broadly claimed N-terminally truncated galectin-3, could not be predicted and would not be expected to be the same as that of an unaltered SEQ ID NO: 1 and the functions and effects of fragments and variants could not be extrapolated from the functions and effects of SEQ ID NO: 1 with a reasonable expectation of success.

Clearly, given the teachings of Bowie et al, Lazar et al, and Burgess et al the effects of undefined changes in the broadly claimed N-terminally truncated galectin-3 could not be predicted without undue experimentation.,. Furthermore, the specification does not teach which amino acids that are critical for the claimed protein to be functionally effective for the claimed effects tumors/cancer, inflammation, and arthritis. Thus the specification provides neither sufficient information nor guidance on how to make the broadly claimed N-terminally truncated galectin-3 that is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis. Thus, it would take undue experimentation for one of ordinary skill in the art to practice the invention as claimed.

2) As drawn to the unpredictability of drug discovery it is well known that the art of that the development of new therapies is highly unpredictable. For example, Gura (Science, 1997, 278:1041-1042, previously cited) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but only 29 have actually been

shown to be useful for chemotherapy (p. 1041, see 1st and 2nd para.). Furthermore, Kaiser (Science, 2006, 313: 1370, previously cited) teaches that 90% of tumor drugs fail in patients; see 3rd col., 2nd to last para. Furthermore, Feldmann and Steinman (Nature, 2005, 435:612-619, previously cited) teach that in the pharmaceutical industry, drugs in only about 5% of the 'small molecule' drug projects end up as approved therapeutics (see p. 614, left col. 1st full para.). Furthermore, Feldmann and Steinmann teach that in selecting targets for treatment of autoimmune disease like rheumatoid arthritis, "A widespread misconception is that every step of the immune or proinflammatory process is a potential therapeutic target. Regrettably, this is not the case. Because most therapeutics only have a partial inhibitory effect, only those molecules that are in short supply (and thus rate-limiting) are likely to be useful targets (see p.612, right col.)." Additionally, Feldmann and Steinman teach that, " Although there is a lot of optimism . . . that many new safe therapies are just around the corner, this hope belies the fact that clinical successes, where the benefits outweigh the risks, are few and far between (see p. 617, right col.)."

Because of the known unpredictability of the art, in the absence of experimental evidence in an appropriate animal model commensurate in scope with the invention claimed, no one skilled in the art would accept the assertion that the claimed composition would be effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis, other than breast cancer, based on the specification as originally filed

3) As drawn to the heterogeneity of cancers, cancers comprise a broad group of malignant neoplasms divided into two categories, carcinoma and sarcoma. The carcinomas

originate in epithelial tissues while sarcomas develop from connective tissues, see Taber's Cyclopedic Medical Dictionary (1985, F.A. Davis Company, Philadelphia, p. 274, previously cited). Given that not all cancers originate from the same tissue types, it is expected and known that cancers originate from different tissue types have different structures as well as etiologies and would present differently. Thus, it would not be predictably expected that a nexus, for example drawn to a connection between N-terminally truncated galectin-3 and breast cancer cells, would be established between two cancer types that arose from different tissue types. Further, it is well known that even two carcinomas that present on the same organ have significant differences in etiology and genetic constitution. For example, Busken, C. et al. (Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No: 850previouly cited), teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract). Furthermore Krontiris and Capizzi (Internal Medicine, 4th Edition, Editor-in-chief Jay Stein, Elsevier Science, 1994 Chapters 71-72, pages 699-729, previously cited) teach that the various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocols.

Given the above, it is clear that it is not possible to predictably extrapolate a correlation between N-terminally truncated galectin-3/SEQ ID NO: 1 therapy in breast cancer to any tumor type or any other diseases which are well known in the art to have different etiologies and pathologies, based on the information in the specification and known in the art without undue experimentation.

4) As drawn to targeting of diseased cells, the N-terminally truncated galectin-3 protein must accomplish several tasks to be effective for therapy. It must be delivered into the circulation that supplies the diseased tissue and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. Also, the target cell must not have an alternate means of survival and function despite action at the proper site for the N-terminally truncated galectin-3. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The N-terminally truncated galectin-3/ may be inactivated *in vivo* before producing a sufficient effect or even binding to the target, for example, by degradation, immunological activation or due to an inherently short half-life of the protein. In addition, the protein may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where it has no effect, circulation into the target area may be insufficient to carry the protein and a large enough local concentration may not be established. Although drawn to antibody immunotherapy, the teachings of White et al. (2001, Ann. Rev. Med., 2001, 52:125-145, previously cited) are relevant to the use of the instant composition for treatment by its binding to target antigens. White et al. teach that for successful targeting and immunotherapy, besides specificity of the antibody for the antigen, other prosperities of the antigen should be considered including the following: (1) the antigen should be present on all or near all of the malignant cells to allow effective targeting and to prevent a subpopulation of antigen-negative cells from proliferating; and (2) whether antigens are shed, modulated, or internalized influences the effectiveness of the administered immunotherapy (i.e. the antibody) (p.125, 2nd para.).

Given what is know in the art and in the absence of additional guidance, for example data showing an effect of the broadly claimed N-terminally truncated galectin-3 on inducing cell death in cancer cells, inhibiting inflammation, or inhibiting symptoms of rheumatoid arthritis, one of skill in the art would not predictably be able to make and used the broadly claimed N-terminally truncated galectin-3 that is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis.

The specification provides insufficient guidance with regard to these issues and provides insufficient working examples which would provide guidance to one skilled in the art and insufficient evidence has been provided which would allow one of skill in the art to predict that the invention will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

In response to the previous rejection under 35 USC 112, first paragraph, Applicants argue that the new claims 38-50 do not recite the terms "according to" or "corresponding to." The Applicants respectfully submit that new independent claim 38 recites, "A composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1"

Applicants argue that what is claimed in the instant application is a specific truncated galectin-3 molecule of 136 amino acids in length having the claimed activities. This molecule is novel and non-obvious and unexpectedly retains the activity of the entire galectin-3C molecule.

Applicants argue that Appendix A is attached to this amendment and response in support of the claimed subject matter.

Applicants' arguments have been considered, but have not been found persuasive because persuasive as the new claims are not limited to a specific truncated galectin-3 molecule of 136 amino acids in length having the claimed activities, but the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143 and the claims are not enabled for the reasons set forth above.

With regard to Appendix A Applicants' arguments have not been found persuasive because no oath or declaration was filed in conjunction with this evidence and the evidence was not considered. When any claim of an application or a patent under reexamination is rejected or objected to, any evidence submitted to traverse the rejection or objection on a basis not otherwise provided for must be by way of an oath or declaration, see 37 CFR 1.132. Furthermore, "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001." Ex parte Gray, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989), see MPEP 716.02 (g).

8. Claims 38-50 are rejected as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis. The broadest reasonable interpretation of the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143 that will be effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis. The genus of N-terminally truncated galectin-3 is highly variant that varies significantly both in structure and function. The description of SEQ ID NO: 1 that is effective to reduce breast tumor size or reduce breast tumor metastasis fails to adequately describe the genus of N-terminally truncated galectin-3 because said genus tolerates members which differ significantly in both structure and function from SEQ ID NO: 1. One of skill in the art can reasonably conclude that applicant was not in possession of a genus of "N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SE Q ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1" that is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis at the time the invention was filed.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the

written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

In the instant case the genus is only described as a definition by function (i.e. reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis), and beyond SEQ ID NO: 1, one of skill in the art cannot readily visualize or recognize the identity of members of the genus in the absence of knowledge as to what that material consists of. Although Gong et al. (Cancer Res. Dec. 1999 59:6239-6245, IDS) teaches that the 11 amino terminal amino acids of full length Galectin-3

results in abolition of the secretion of galectin-3, loss of nuclear localization, and reduced carbohydrate function, see Abstract, given the unpredictability of predicting protein function from structure set forth in section 7 above, one of skill in the art cannot readily envision the genus of " N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1 that is effective to reduce tumor size, reduce tumor metastasis, induce cell death in cancer cells, inhibit inflammation, or inhibit symptoms of rheumatoid arthritis.

In response to the previous rejection under 35 USC 112, first paragraph, written description, Applicants argue that new 38-50 overcome the rejection based on 35 U.S.C. §112, first paragraph. New claim 38 recites "truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1." Applicants argue that new independent claim 38 does not recite "N- terminally truncated galectin-3 that begins with any of the amino acid residues from Gly-1 through Arg-22 of S EQ I D NO:1 and extends to any of the amino acid residues from Asp-134 through Ile-143 of SEQ ID NO: 1..." The Applicants respectfully request removal of the rejection based on 35 U.S.C. 112, first paragraph.

Applicants argue that, in addition, they have attached Appendix A in support of the claimed subject matter. Appendix A, Figs. 1A and 1B illustrate the that N-terminally truncated Galectin-3 consisting of Leu-7 to Ile-143 of SEQ ID NO: 1, was nearly identical in activity to that of the N- terminally truncated Galectin-3 of SEQ ID NO: 1 consisting of Gly-1 to Ile-143 of SEQ ID NO: 1. The binding was determined by fluorescence polarization analysis using a fluorescently-labeled carbohydrate ligand where there is increased polarization of the fluorescence-labeled molecule when it is bound to the protein. These data illustrate that the

smaller of the two N-terminally truncated galectin-3 molecules, that both lack the multimerization region, retains carbohydrate binding functions as an inhibitor as well, or better than the larger N-terminally truncated protein.

Applicants' arguments have been considered, but have not been found persuasive because persuasive as the new claims are not limited to a specific truncated galectin-3 molecule of 136 amino acids in length having the claimed activities, but the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143 and the broadly claimed N-terminally truncated galectin-3 does not have written description for the reasons set forth above.

With regard to Appendix A Applicants' arguments have not been found persuasive because no oath or declaration was filed in conjunction with this evidence and the evidence was not considered. When any claim of an application or a patent under reexamination is rejected or objected to, any evidence submitted to traverse the rejection or objection on a basis not otherwise provided for must be by way of an oath or declaration, see 37 CFR 1.132. Furthermore, "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001." Ex parte Gray, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989

9. Claims 38-50 are rejected as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The limitation of a composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to induce cell death in cancer cells, or wherein the composition consists of one or more additional agents, wherein the one or more additional agents are selected from the group consisting of an anti-inflammatory agent and an anti-cancer agent claimed in 38-50 has no clear support in the specification and the claims as originally filed. Applicants pointed to support for the new claims in the specification page 1 lines 16-22; page 7 line 21 to page 8 line 28; page 19 lines 16- 29; page 23 lines 10-12; page 24 line 15 to page 32 line 10; page 39 line 17 to page 40 line 2; page 41 lines 1-23; and page 74 line 27 to page 77 line 20 and Claims 1-4, 7 and 11. A review of the specification discloses support for compositions for treating cancer and conditions or disease involving inflammation, undesirable immunity and infection and a composition containing N-terminally truncated galectin-3 and homologues thereof (page 1 lines 16-22), a description of juvenile idiopathic arthritis, the expression of galectin-3 in arthritis, and the effect of galectin-3 on innate immunity and acute inflammation (page 7 line 21 to page 8 line 28); The N-terminally truncated galectin-3 proteins include truncated forms of the human recombinant galectin-3 protein designated SEQ ID NO. 3. This definition is not limited by the method(s) by which the proteins are obtained, and includes all the N-terminally truncated galectin-3 molecules otherwise within the definition, whether purified from nature source, obtained by recombinant DNA technology, synthesized, or prepared by any combination of these and/or other techniques

known to those of skill in the art. Thus, there are provided N-terminally truncated human galectin-3 molecules that differ slightly in length. The molecules can be somewhat longer or shorter than the 143 amino acid residue N-terminally truncated galectin-3 that is lacking the N-terminal 107 amino acids. The molecules have essentially the same ability to inhibit the carbohydrate binding and multimerization of galectin-3 and, therefore, inhibit tumorigenicity and metastasis and other diseases in vivo, including, but not limited to inflammation resulting from arthritis and cancer (page 19 lines 16- 29); use of the C-terminal domain of galectin-3 for use as a therapeutic agent and in a slow release form (page 23 lines 10-12); an N-terminally truncated variant having at least the qualitative biological activity as defined herein and having, for example, at least about 75%, and preferably at least 90%, amino acid homology with the portions that it contains of the polypeptide of SEQ ID NO: 1. The variant amino acid sequence preferably shares at least 80%, more preferably, greater than 85% sequence homology with the portion that it contains of the sequence of SEQ ID NO: 1. However, a galectin-3 variant or related compound can exhibit less than 50% sequence homology with the sequence of SEQ ID NO: 1 and still retain the characteristics of a galectin-3 variant as described herein. In this regard, it is understood that amino acids can be substituted on the basis of side chain bulk, charge and/or hydrophobicity, PEGylated forms of the truncated Galectin-3 wherein, specific PEG derivatives react with thiols such as the amino acid residue cysteine . These include PEG-ortopyridyl-disulphide, PEG-malemide, and PEG-vinylsulphone. In a preferred method, N-terminally truncated human galectin-3 that is lacking the 107 amino acids on the N-terminus, or is similar in function, is derivatized on the single cysteine in the sequence (SEQ ID NO. 1). Alternatively, the N-terminally truncated human galectin-3 can be produced with one or more cysteine residues on

the N-terminus as described above (SEQ ID NO. 2). Then one or more of the cysteine residues is derivatized with a thiol reactive PEG derivative. (page 24 line 15 to page 32 line 10); formulations and methods of administration of pharmacological formulations (page 39 line 17 to page 40 line 2): properties of N-terminally truncated galectin-3 (page 41 lines 1-23); hypothetical experiments to test the effect of N-terminally truncated galectin-3 on arthritis (page 74 line 27 to page 77 line 20); A composition comprising an effective amount of N-terminally truncated galectin-3 and a pharmaceutically acceptable carrier, wherein said N-terminally truncated galectin-3 has a sequence according to SEQ ID NO: 1 and analogues thereof, is present in an amount sufficient to reduce tumor size, for use in for treating cancer (original Claims 1-4 and 7); A treatment for cancer and inflammation comprising an effective amount of N-terminally truncated galectin-3 according to claim 1, and a pharmaceutically acceptable carrier (original claim 11)

The suggested support is not found persuasive because there is nothing in the specification to suggest the specific N-terminally truncated galectin-3 that begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, wherein the N-terminally truncated galectin-3 is effective to induce cell death in cancer cells, wherein the composition consists of one or more additional agents, wherein the one or more additional agents are selected from the group consisting of an anti-inflammatory agent and an anti-cancer agent. The subject matter claimed in claims 38-50 broadens the scope of the invention as originally disclosed in the specification.

Claim Rejections - 35 USC § 103

10. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No, 6,967,021 (Panjawani et al. April 27, 2001) in view of Veronese (Biomaterials, March 2001, 22:405-17) and in further view of Kinstler et al. (Pharm. Res. 1996 13: 996-1002).

US Patent No, 6,967,021 teaches as set forth above, but does not teach attaching PEG molecules 3 on a Cys residue added to the N-terminus of SEQ ID NO: 1. US Patent No, 6,967,021 teaches using galectin-3/SEQ ID NO: 1 for the treatment of epithelial wounds, see Abstract and claims.

Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, see p. 405-right col. Veronese teaches that PEG conjugation of a protein can maintain its biological functions while inhibiting antibodies, antigen processing cells, and proteolytic enzyme activities toward the protein, see p. 406-left col. Veronese teaches PEGylation of proteins using rare thiols like cysteine, see p. 410 and figure 9. Veronese teaches that the rare cysteine residue may be introduced at the desired position of the sequence by genetic engineering, a strategy that offers the conditions for site directed PEGylation, see p. 410-1st col.

Kinstler et al. teaches that addition of a PEG group to the N-terminal residue of the protein rhG–CSF increase the proteins circulation time and had no effect on its activity, see p. 996-1st col.

It would have been *prime facie* obvious for one of skill in the art to conjugate galectin-3/SEQ ID NO: 1 taught by US Patent No, 6,967,021 with PEG because Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, thus one of skill in the art would have been motivated to attach PEG as describe by Veronese to enhance the

therapeutic potential of galectin-3/SEQ ID NO: 1 taught by US Patent No, 6,967,02 in the treatment epithelial wounds.

Additionally, it would have been *prime facie* obvious for one of skill in the art to one skill in the art and one would have been motivated to add a cysteine residue at the N-terminus of the galectin-3 of Panjawani et al. because Veronese teaches that the rare cysteine residue may be introduced at the desired position of the sequence by genetic engineering, a strategy that offers the conditions for site directed PEGylation and Kinstler et al. teach that adding a PEG group increases circulation time and has no effect on activity. Furthermore, the additional cysteine residue would have increased the chance of effective PEGylation of the protein. Thus, given the high level of skill in the art and successful making and using of proteins that are PEGylated at cysteine residues and the N-terminus and given the benefits of such PEGylation, one of skill in the art would have been motivated with a reasonable expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 38-50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,770,622 in view of Veronese (Biomaterials, March 2001, 22:405-17), and in further view of Kinstler et al. (Pharm. Res. 1996 13: 996-1002).

It is noted that the recitation of the uses of the composition in claim 7 is merely suggestive of intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which are the proteins comprising the claimed N-terminally truncated galectin-3.

It is noted that , given their broadest reasonable interpretation the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a polypeptide consisting of SEQ ID NO: 1 is protein comprising a protein starting with Leu-7 and extending to Ile-143 of SEQ ID NO: 1. Additionally, given that claim 2 is drawn to using SEQ ID NO: 1 to reduce metastasis and tumor size and the specification contemplates the composition comprising additional chemotherapeutic agents, it would be obvious to one of skill in the art to add anti-cancer agents as combination chemotherapy is routine in the art. Furthermore, given that claim 2 is drawn to using SEQ ID NO: 1 to reduce metastasis and tumor size and given that SEQ ID NO: 1 of U.S. Patent No. 6,770,622 and the instant specification are identical, the claimed product appears to be the same as the prior art

product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, see p. 405-right col. Veronese teaches that PEG conjugation of a protein can maintain its biological functions while inhibiting antibodies, antigen processing cells, and proteolytic enzyme activities toward the protein, see p. 406-left col. Veronese teaches PEGylation of proteins using rare thiols like cysteine, see p. 410 and figure 9.

Kinstler et al. teaches that addition of a PEG group to the N-terminal residue of the protein rhG–CSF increase the proteins circulation time and had no effect on its activity, see p. 996-1st col.

It would have been *prime facie* obvious for one of skill in the art to conjugate SEQ ID NO: 1 taught by US Patent No, 6,770,622 with PEG because Veronese teaches that PEG conjugation is performed for enhancing the therapeutic potential of proteins, thus one of skill in the art would have been motivated to attach PEG as describe by Veronese to enhance the therapeutic potential of SEQ ID NO: 1 taught by US Patent No, 6,770,622 in the treatment cancer. One would have been motivated to attach the PEG molecules a Cys-66 as this is the only cysteine in galectin-3, truncated or full length.

Additionally, it would have been *prime facie* obvious for one of skill in the art to one skill in the art and one would have been motivated to add a cysteine residue at the N-terminus of the galectin-3 of US Patent No, 6,770,622 because Veronese teaches that the rare cysteine residue may be introduced at the desired position of the sequence by genetic engineering, a strategy that offers the conditions for site directed PEGylation and Kinstler et al. teach that adding a PEG group increases circulation time and has no effect on activity. Furthermore, the additional cysteine residue would have increased the chance of effective PEGylation of the protein. Thus, given the high level of skill in the art and successful making and using of proteins that are PEGylated at cysteine residues and the N-terminus and given the benefits of such PEGylation, one of skill in the art would have been motivated with a reasonable expectation of success.

Applicants argue that new claims 38-50 overcome the double patenting rejection by recitation of "A composition consisting of N-terminally truncated galectin-3, wherein the truncated galectin-3 begins with Leu-7 of SEQ ID NO: 1 and extends to Ile-143 of SEQ ID NO: l," elements of new independent claim 38.

Applicants' arguments have been considered, but have not been found persuasive as the new claims are not limited to a truncated galectin-3 protein consisting of residues 7-143 of SEQ ID NO: 1, but the claims encompasses a protein comprising a protein starting with Leu-7 and extending for any length to Ile-143 of SEQ ID NO: 1 with any length or type of sequence in between Leu-7 and Ile-143. Thus, the protein claimed by US Patent No, 6,770,622 is encompassed by the claimed protein.

Claim Objections

12. Claims 49 and 50 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 49 and 50 are broader than 38 because claim 38 is drawn to a composition consisting of N-terminally truncated galetin-3 and a pharmaceutically acceptable carrier and claims 49 and 50 add in one or more additional agents that to a composition that consists of only two components.

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PETER J. REDDIG whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Examiner, Art Unit 1642